IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of: Rambhatla L., et al.

Serial No.:

[to be assigned]

Filing Date: October 31, 2001

For:

HEPATOCYTE LINEAGE CELLS DERIVED

FROM PLURIPOTENT STEM CELLS

INFORMATION DISCLOSURE STATEMENT **PURSUANT TO 37 CFR § 1.98(d)**

Assistant Commissioner for Patents Washington, D.C. 20231

Dear Sir:

The information listed in the accompanying form PTO-1449 may be material to examination of this application and are submitted in compliance with the duty of disclosure under 37 CFR § 1.56. The Examiner is requested to make this information of record in the application.

Copies of the information are not provided herewith, but were previously filed in parent application 09/718,308, to which this application claims priority under 35 USC § 120. The Examiner is respectfully directed to the file for application 09/718,308 to access the information listed on the accompanying form PTO-1449. This is in compliance with the provisions of 37 CFR § 1.98(d).

PATENT Docket: 093/004p

This Information Disclosure Statement is not to be construed as a representation that a full search for relevant information has been made, or that the information listed on the accompanying PTO-1449 is material to patentability of the claimed invention under 37 CFR § 1.56(b).

Respectfully submitted,

Registration No. 40,253

GERON CORPORATION 230 Constitution Drive Menlo Park, CA 94025 Telephone: (650) 473-7715

Fax: (650) 473-8654

October 31, 2001

Information Disclosure Statement By Applicant

(Use Several Sheets if Necessary)

Docket: 093/004

U.S.N. To be assigned

Title: Hepatocyte Lineage Cells Derived from Pluripotent Stem Cells

Inventors: Rambhatla, L., et al.

Filing Date: October 31, 2001

Group: To be assigned

assigned 200126

U.S. Patent Documents

Examiner Initial	Ref.	Patent No.	Filing Date	Issue Date	Class/ Subclass	Inventors:	Title:
	Α	5,030,105	11/15/89	7/9/91	435/29	Kuri-Harcuch, W., et al.	Process For The Long-Term Surviving Culture Of Hepatocytes
	В	5,532,156	10/8/93	7/2/96	435/240.2	Talbot, N., et al.	Hepatocyte Cell Line Derived From The Epiblast Of Pig Blastocysts
	С	5,559,022	1/26/95	9/24/96	435/240.2	Naughton, B.A., et al.	Liver Reserve Cells
	D	5,576,207	6/24/94	11/19/96	435/240.2	Reid, L.M., et al.	Method O Expanding Hepatic Precursor Cells
	Е	5,763,255	1/25/95	6/9/98	435/240.23	Swiderek, M.S., et al.	Inducing Epithelial Cell Differentiation With Dried Native Fibrillar Collagen
	F	5,869,243	3/5/96	2/9/99	435/6	Jauregui, H.O., et al.	Immortalized Hepatocytes
	G	6,017,760	10/10/95	1/25/00	435/378	Jauregui, H.O., et al.	Isolation and Culture Of Porcine Hepatocytes

Foreign Patent or Published Foreign Patent Application

Examiner	Τ_,	Document	Publ.	Juris-	Title:		Translation	
Initial	Ref.	No.	Date	diction	Title.	Yes	No	
	Н	WO 95/12665	5/11/95	PCT	Embryonic Stem Cells Capable Of Differentiating Into Desired Cell Lines			
	ı	WO 97/47307	12/18/97	PCT	Use Of Histone Deacetylase Inhibitors To Activate Transgene Expression			
	J	EP 0 827 742 A1	3/11/98	EP	Use Of Histone Deacetylase Inhibitors For Treating Fribosis Or Cirrhosis			
	к	EP 0 827 743 A1	3/11/98	EP	Use Of Histone Decarboxylase Inhibitors For Treating Fibrosis			
· · · · · · · · · · · · · · · · · · ·	L	WO 99/23885	5/20/99	РСТ	Methods For The Use Of Inhibitors Of Co-Repressors For The Treatment Of Neoplastic Diseases			
	М	WO 99/37150	7/29/99	PCT	Transcription Therapy For Cancers			
	N	EP 0 953 633 A1	11/3/99	EP	Cell Culturing Method And Medium For Producing Proliferated, Normal, Differentiated Human Liver Cells			
	0	WO 00/03001	1/20/00	PCT	Liver Stem Cell			
	Р	WO 00/18239	4/6/00	РСТ	Reversibly Immortalized Hepatocytes And Methods Of Use			
	Q	WO 00/22098	4/20/00	РСТ	Porcine Occytes with Improved Developmental Competence			
	R	WO 00/43498	7/27/00	PCT	Human Liver Progenitors			

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Other Documents

		Other Docume	ento			
Examiner Initial	Ref.	Autho	or, Title, Source, Date			
muai	S		nd long-term storage of primary human hepatocytes with recovery ", Cell Transplantation, 4(6):579-586 (1995)			
	т	Agelli, M., et al., "Putative liver progenitor cells: co 29:205-217 (1997)	onditions for long-term survival in culture", Histochemical Journal,			
	U	Alison, M. "Liver stem cells: a two compartments	system", Cell Biology, 10:710-715 (1998)			
	v	Baribault, H., et al., "Dexamethasone and dimeth	ylsulfoxide as distinct regulators of growth and differentiation of 129(1):77-84 (1986)			
	w	Block, G.D., et al., "Population expansion, clonal hepatocytes induced by HGF/SF, EGF and TGF-	growth, and specific differentiation patterns in printary cultures of in a chemically defined (HGM) medium", <i>J Cell Bio.</i> , 132 (6)1133-			
	×	Blouin, MJ., et al., "Specialization switch in different to the control of the co	entiating embryonic rat liver progenitor cells in response to sodium			
	Y	Brill, S., et al., "Expansion conditions for early he	patic progenitor cells from embryonal and neonatal rat livers", Dig			
	z	Buommino, E., et al., "Sodium butyrate/retinoic acid costimulation induces apoptosis-independent growth arrest and cell differentiation in normal and ras-transformed seminal vesicle epithelial cells unresponsive to retinoic acid", and cell differentiation in normal and ras-transformed seminal vesicle epithelial cells unresponsive to retinoic acid", and cell differentiation in normal and ras-transformed seminal vesicle epithelial cells unresponsive to retinoic acid", and cell differentiation in normal and ras-transformed seminal vesicle epithelial cells unresponsive to retinoic acid", and cell differentiation in normal and ras-transformed seminal vesicle epithelial cells unresponsive to retinoic acid", and cell differentiation in normal and ras-transformed seminal vesicle epithelial cells unresponsive to retinoic acid", and cell differentiation in normal and ras-transformed seminal vesicle epithelial cells unresponsive to retinoic acid", and cell differentiation in normal and ras-transformed seminal vesicle epithelial cells unresponsive to retinoic acid", and cell differentiation in normal and ras-transformed seminal vesicle epithelial cells unresponsive to retinoic acid", and cell differentiation in the cell differ				
	AA	Chen, WY., et al., "Reactivation of silenced, virally transduced genes by inhibitors of histone deacetylase", <i>Proc. Natl. Acad. Sci. USA</i> , 94 :5798-5803 (5/97)				
	AB	Coghlan, A., "Highly Cultured", New Scientist, A	ug. 19, 2000			
	AC	Coleman W.B., et al., "Development of dexamethasone-inducible tyrosine aminotransferase activity in WB-F344 r. Coleman W.B., et al., "Development of dexamethasone-inducible tyrosine aminotransferase activity in WB-F344 r. Coleman W.B., et al., "Development of dexamethasone-inducible tyrosine aminotransferase activity in WB-F344 r. Coleman W.B., et al., "Development of dexamethasone-inducible tyrosine aminotransferase activity in WB-F344 r. Coleman W.B., et al., "Development of dexamethasone-inducible tyrosine aminotransferase activity in WB-F344 r. Coleman W.B., et al., "Development of dexamethasone-inducible tyrosine aminotransferase activity in WB-F344 r. Coleman W.B., et al., "Development of dexamethasone-inducible tyrosine aminotransferase activity in WB-F344 r. Coleman W.B., et al., "Development of dexamethasone-inducible tyrosine aminotransferase activity in WB-F344 r. Coleman W.B., et al., "Development of dexamethasone-inducible tyrosine aminotransferase activity in WB-F344 r. Coleman W.B., et al., "Development of the presence of sodium butyrate", J Cell Physiol, 161(3):463-469 (12/94)				
	AD	Davis, MG., et al., "Involvement of gialpha2 in sodium butyrate-induced erythroblastic differentiation of K302 cens, Davis, MG., et al., "Involvement of gialpha2 in sodium butyrate-induced erythroblastic differentiation of K302 cens, p. 1.1(248) Pt2-455-461 (3/00)				
	AE	Devereux, T.R., et al., "DNA methylation analysis of the promoter region of the human telomerase reverse				
	AF	Enat, R., et al., "Hepatocyte proliferation in vitro: Its dependence on the use of serum-free normality defined the series of extracellular matrix". Proc. Natl. Acad. Sci. USA, 81:1411-1415 (3/84)				
	AG	Engelmann, G.L., et al., "Effect of sodium butyrate on primary cultures of adult rat nepatocytes," In Vitro dell 200				
	AH	Falasca, L., et al., "The effect of retinoic acid on the re-establishment of differentiated nepatocyte prieriotype in				
	Al	Germain, L., et al., "Biliary epithelial and hepatocytic cell lineage relationships in embryonic rat liver as determined by the differential expression of cytokeratins, ∝-fetoprotein, albumin, and cell surface-exposed components" by the differential expression of cytokeratins, ∝-fetoprotein, albumin, and cell surface-exposed components are the components.				
	AJ	Germain, L., et al., "Promotion of growth and differentiation of rat ductular oval cells in primary culture", Cancer				
	AK	Gillenwater, A., et al., "Effects of sodium butyrate on growth, differentiation, and apoptosis in nead and neck				
	AL	Gladhaug, I.P., et al., "Effects of butyrate on epidermal growth factor receptor binding, morphology, and DIVA				
	AM	Graham, K.A., et al., "Sodium butyrate induces differentiation in breast cancer cell lines expressing the estroger				
_	AN	Grisham, J.W., et al., "Liver stem cells", Stem	Cells, 233-282 (1997)			
Examiner			Date Considered			

Examiner: Initial if citation considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. PTO-1449 -- Page 2

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Examiner Initial	Ref.	Author, Title, Source, Date	Ď
	AO	Guixiang, T., et al., "Different effects of cyclic AMP and butyrate on eosinophilic differentiation, apoptosis and bol expression of a human eosinophilic leukemia cell line, EoL-1", Hematol Oncol, 14(4):181-92 (12/96)	-2
	AP	Jeng, J.H., et al., "Effects of butyrate and propionate on the adhesion, growth, cell cycle kinetics, and protein synthesis of cultured human gingival fibroblasts", <i>J Periodontol</i> , 70 (12):1435-1442 (12/99)	
	AQ	Kamitani, H., et al., "Regulation of 12-lipoxygenase in rat intestinal epithelial cells during differentiation and apoptosis induced by sodium butyrate", Arch Biochem Biophys, 368(1):45-55 (8/1/99)	
	AR	Kosugi, H., et al., "Histone deacetylase inhibitors are the potent inducer/enhancer of differentiation in acute myelleukemia: a new approach to anti-leukemia therapy", <i>Leukemia</i> , 13:1316-1324 (1999)	
	AS	Lazaro, C.A., et al., "Generation of hepatocytes from oval cell precursors in culture", Cancer Res, 58:5514-5522 (12/1/98)	
	АТ	Li, J., et al., "Mammalian hepatocyte differentiation requires the transcription factor HNF-4x", Genes & Dev, 14:464-474 (2000)	
	AU	Matsui, T., et al., "Induction of catecholamine synthesis in human neuroblastoma cells by replication inhibitors ar sodium butyrate", <i>Brain Res</i> , 843 (1-2):112-117 (10/2/99)	
	AV	McBain, J., et al., "Apoptotic death in adenocarcinoma cell lines induced by butyrate and other histone deacetyla inhibitors", <i>Biochem Pharm</i> , 53 :1357-1368 (1997)	
	AW	Michalopoulos, G.K., et al., "Morphogenetic events in mixed cultures of rat hepatocytes and nonparenchymal cel maintained in biological matrices in the presence of hepatocyte growth factor and epidermal growth factor", Hepatology, 29(1):90-100 (1999)	
	AX	Mitaka, T., et al., "Redifferentiation of proliferated rat hepatocytes cultured in L15 medium supplemented with EG and DMSO", In Vitro Cell Dev. Biol., 29A:714-722 (9/93)	¥F
	AY	Mitaka, T., "The current status of primary hepatocyte culture", Int. J. Exp. Path, 79:393-409 (1998)	
	AZ	Niki, T., et al., "A histone deacetylase inhibitor, trichostatin A, suppresses myofibroblastic differentiation of rat hepatic stellate cells in pimary culture", <i>Hepatology</i> , 29 (3):858-867 (1999)	
	ВА	Pack, R., et al., "Isolation, biochemical characterization, long-term culture, and pheotype modulation of oval cells from carcinogen-fed rats", Exp Cell Res, 204(2):198-209 (1993)	ŝ
	ВВ	Pagan, R., et al., "Effects of growth and differentiation factors on the epithelial-mesenchymal transition in culture neonatal rat hepatocytes", <i>J of Hepatology</i> , 31 :859-904 (1999)	id .
	вс	Perez, R., et al., "Sodium butyrate upregulates Kupffer cell PGE2 production and modulates immune function", Surg Res, 78(1):1-6 (7/15/98)	
	BD	Perrine, SP., et al., "A short-term trial of butyrate to stimulate fetal-globin-gene expression in the beta-globin disorders", N Engl J Med, 328(2):81-86, (1/14/93)	
	BE	Perrine, SP., et al., "Butyrate derivatives. New agents for stimulating fetal globin production in the beta-globin disorders", Am J Pediatr Hemotol Oncol, 16(1):67-71 (2/94)	
	BF	Reynolds, S., et al., "Differentiation-inducing effect of retinoic acid, difluoromethylornithine, sodium butyrate and sodium suramin in human colon cancer cells", Cancer Lett, 134(1):53-60 (12/11/98)	
	BG	Rivero JA., et al., "Sodium butyrate stimulates PKC activation and induces differential expression of certain PKC isoforms during erythroid differentiation", <i>Biochem Biophys Res Commun</i> , 248 (3):664-668 (7/30/98)	;
	вн	Rocchi, P., et al., "Effect of butyrate analogues on proliferation and differentiation in human neuroblastoma cell lines", <i>Anticancer Res</i> , 18 (2A):1099-103 (3/98)	
	ВІ	Rogler, LE., "Selective bipotential differentiation of mouse embryonic hepatoblasts in vitro", Am J Pathol, 150(2):591-602 (1997)	
	BJ	Runge, D., et al., "STAT 1 alpha/1 beta, STAT 3 and STAT 5: Expression and Association with c-MET and EGF Receptor in Long-Term Cultures of Human Hepatocytes", <i>Biochemical and Biophysical Research Communicatio</i> 265 :376-381 (1999)	- ons,

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	вк	Saito, H., et al., "Differentiating effect of sodium butyrate on human hepatoma cell lines PLC/PRF/5, HCC-M and HCC-T", Int J Cancer, 48(2):291-296 (5/10/91)
	BL	Sanchez, A., et al., "Transforming growth factor-B (TGF-B) and EGF promote cord-like structures that indicate terminal differentiation of fetal hepatocytes in primary culture", Exp Cell Res, 242:27-37 (1998)
	ВМ	Schultz, RM., et al., "Reprogramming of gene expression during preimplantation development", <i>J of Exp Zoology</i> (Mol Dev Evol), 285 :276-282 (1999)
	BN	Siavoshian, S., et al., "Butyrate and trichostatin A effects on the proliferation/differentiation of human intestinal epithelial cells: induction of cyclin D3 and p21 expression", <i>Gut</i> , 46 (4):507-14 (4/2000)
	во	Simon, B., et al., "Transient transcriptional activation of gastrin during sodium butyrate-induced differentiation of islet cells", Regul Pept, 70(2-3):143-8 (6/18/97)
	ВР	Staecker, JL., et al., "Stimulation of DNA synthesis in primary cultures of adult rat hepatocytes by sodium butyrate", Biochem Biophys Res Commun, 147(1):78-85 (8/87)
	BQ	Staecker, JL., et al., "The effect of sodium butyrate on tyrosine aminotransferase induction in primary cultures of normal adult rat hepatocytes", Arch Biochem Biophys, 261(2):291-8 (3/88)
	BR	Staecker, JL., et al., "Sodium butyrate preserves aspects of the differentiated phenotype of normal adult rat hepatocytes in culture", <i>J Cell Physiol</i> , 135(3):367-76 (1988)
	BS	Strain, A., "Ex vivo liver cell morphogenesis: one step nearer to the bioartificial liver", <i>Hepatology</i> , 29 (1):288-290 (1/99)
	вт	Sun, SH., et al., "Altered phospholipid metabolism in sodium butyrate-induced differentiation of C6 glioma cells", Lipids. 32(3):273-82 (3/97)
	BU	Tamagawa, K., et al., "Proanthocyanidins from barley bran potentiate retinoic acid-induced granulocytic and sodium butyrate-induced monocytic differentiation of HL60 cells", <i>Biosci Biotechnol Biochem</i> , 62 (8):1483-7 (8/98)
	BV	Tanaka, T., et al., "Adenovirus-mediated prodrug gene therapy for carcinoembryonic antigen-producing human gastric carcinoma cells in vitro", Cancer Res, 56(6):1341-5 (3/96)
	BW	Tateno, C., et al., "Growth and differentiation of adult rat hepatocytes regulated by the interaction between parenchymal and non-parenchymal liver cells", <i>J of Gasto and Hepatology</i> , 13:S83-92 (1998)
	вх	Tateno, C., et al., "Growth potential and differentiation capacity of adult rat hepatocytes in vitro", Wound Repair and Regeneration, 7(1):36-44 (1999)
	BY	Wang, G., et al., "Transforming growth factor-beta 1 acts cooperatively with sodium n-butyrate to induce differentiation of normal human keratinocytes", Exp Cell Res, 198(1):27-30 (1/92)
	BZ	Watkins, SM., et al., "Butyric acid and tributyrin induce apoptosis in human hepatic tumour cells", <i>J Dairy Res</i> , 66(4):559-67 (11/99)
	CA	Yabushita, H., et al., "Effects of sodium butyrate, dimethylsulfoxide and dibutyryl cAMP on the poorly differentiated ovarian adenocarcinoma cell line AMOC-2", Oncol Res, 5(4-5):173-82 (1993)
	СВ	Yamada, K., et al., "Effects of butyrate on cell cycle progression and polyploidization of various types of mammalian cells", <i>Biosci Biotechnol Biochem</i> , 56 (8):1261-5 (8/92)
	СС	Yoon, J-H., et al., "Augmentation of Urea-synthetic Capacity by Inhibition of Nitric Oxide Synthesis in Butyrate- Induced Differentiated Human Hepatocytes", FEBS Letters, 474:175-178 (2000)
	CD	Yoon, J-H., et al., "Development of a non-transformed human liver cell line with differentiated-hepatocyte and ureasynthetic functions: applicable for bioartificial liver", Int. J. of Artifical Organs, 22:769-777(1999)
	CE	Yoshizawa, T., et al., "Dimethylsulfoxide maintains intercellular communication by preserving the gap junctional protein connexin32 in primary cultured hepatocyte doublets from rats", <i>J of Gastro and Hepat</i> , 12:325-330 (1997)
	CF	Zvibel, I., et al., "Phenotypic characterization of rat hepatoma cell lines and lineage-specific regulation of gene expression by differentiation agents", <i>Differentiation</i> , 63 :215-223 (1998)

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